Screening, diagnosis and monitoring of sarcopenia

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Narrative Review

Screening, diagnosis and monitoring of sarcopenia: When to use which tool?

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SUMMARY

Background & aims: Sarcopenia is a muscle disorder associated with loss of muscle mass, strength and function. Early screening, diagnosis and treatment may improve outcome in different disease conditions. A wide variety of tools for estimation of muscle mass is available and each tool has specific technical requirements. However, different investigational settings and lack of homogeneity of populations influence the definition of gold standards, proving it difficult to systematically adopt these tools. Recently, the European Working Group on Sarcopenia in Older People (EWGSOP) published a revised recommendation (EWGSOP-2) and algorithm for using tools for screening and diagnosing sarcopenia. However, agreement of the EWGSOP2 criteria with other classifications is poor and although an overview of available tools is valuable, for the purpose of clinical decision-making the reverse is useful; a given scenario asks for the most suitable tools.

Results: Tools were identified for screening, diagnostics and longitudinal monitoring of muscle mass. For each of these clinical scenarios the most appropriate tools were listed and for each technique their usability is specified based on sensitivity and specificity. Based on this information a specific recommendation is made for each clinical scenario.

Conclusion: This narrative review provides an overview of currently available tools and future developments for different clinical scenarios such as screening, diagnosis and longitudinal monitoring of alterations in muscle status. It supports clinical decision-making in choosing the right tools for muscle mass quantification depending on the need within a given clinical scenario as well as the local availability and expertise.

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1. Introduction

Sarcopenia is a progressive skeletal muscle disorder associated with health risks such as physical dysfunction, falls, fractures and mortality [1,2]. A meta-analysis of the world's population stated that the prevalence of sarcopenia is roughly 10% in males and females, with higher prevalence among non-Asian individuals [3]. Prevalence may vary in populations as different cut-off values for diagnosing sarcopenia are suggested by prominent research consortia worldwide [1,2,4–6]. Sarcopenia was initially described only in the elderly population as loss of muscle mass and strength with advancing age [7]. Since sarcopenia is now considered to be a muscle disease inducing muscle failure, guidelines have included both loss of strength and muscle function in the adapted definitions [4–6]. New evidence suggests that sarcopenia is also a concern among the obese and the chronically ill [8–11]. This means that the actual number of patients at risk for adverse outcomes is substantially higher than previously found.

Early identification and adequate diagnosis of sarcopenia is important, as poor muscle status may lead to significant health impairments. Diagnosing sarcopenia requires reliable quantification of muscle mass with valid, repeatable and cost-effective tools. A wide variety of tools is available, yet lack of homogeneity of populations and varying investigational settings make it difficult to implement these tools systematically [12]. Recently, the European Working Group on Sarcopenia in Older People (EWGSOP) published a revision of the previous criteria (EWGSOP2) and an algorithm for using tools for screening and diagnosing sarcopenia [1,2]. These criteria increased the interest in writing this narrative review, however, comparison of these criteria with other definitions is poor. In the GLISTEN study the EWGSOP2 criteria were compared with the Foundation for the Nationals Institutes of Health (FNIH) criteria [13]. Although the EWGSOP2 criteria were shown to have the highest predictive value for 3-year mortality in hospitalized patients, agreement between the two definitions was poor [13]. In another study in community-dwelling elderly, agreement with four other modalities, including the first version of the EWGSOP criteria, was also poor [14]. The use of muscle strength criteria in the EWGSOP2 was recently shown to influence the outcome in defining sarcopenia due to significant variation [2,15] providing a possible explanation for the poor agreement. In addition, although an overview of available tools is valuable, for the purpose of clinical decision-making the reverse is useful; a given scenario or clinical demand asks for the most suitable tools. In this narrative review, three distinct areas, which are referred to as clinical scenarios, are identified: screening for sarcopenia, diagnosis of sarcopenia, and longitudinal monitoring of sarcopenia to detect the effects of an intervention.

Because the current techniques show different drawbacks, promising new techniques, such as HD-EMG and microwave imaging are being developed [16]. These techniques improve or replace already existing tools for diagnosis of poor muscle function, but also for repeated measurements to monitor muscle mass.

The context of each paragraph is described by clinical experts in order to give an inclusive and extensive overview of different tools and promising research parameters. This narrative review gives clinical scenarios including their respective technical aspects, their validity and their (dis)advantages. The aim of this review is to provide a variety of tools appropriate for each stage of assessment and to identify new and promising techniques.

2. Clinical scenarios

Recommendations on different clinical scenarios including screening, diagnostic imaging and assessment and monitoring of treatment effects are given.

2.1. Screening tools

Adequate screening tools improve early identification of conditions, creating opportunities for early detection of patients at risk for muscle decline. Screening tests require dichotomous outcome rather that a detailed description. For screening instruments tests with high sensitivity are preferred [12]. In addition to the high sensitivity, screening tools need to be easy to use, fast, non-invasive, and cheap [17].

2.1.1. SARC-F

The SARC-F questionnaire is a self-reporting five-part survey to screen patients for sarcopenia. Initially developed in 2012 by Malmstrom et al. as rapid diagnostic test for sarcopenia [18]. Although developed as a diagnostic tool, it is currently the most validated and adapted screening survey for sarcopenia [19–28]. Its components comprise self-reporting of: strength, assistance with walking, rise from a chair, climb stairs and falls [18] as shown in table 1 (Appendix). High scores are associated with Activity of Daily Living (ADL) deficits, decreased strength and physical performance [19]. Quick and easy to use, the SARC-F does not require additional explanation by a physician when completed by the patient. It can be used in various clinical settings. The SARC-F has a relatively low to mediocre sensitivity and very high specificity to predict sarcopenia [21,22,24]. Its sensitivity, ranging between 3.8% and 33.3% is a serious disadvantage since many sarcopenic patients may be missed [1,2,29]. Due to its low sensitivity, variations on the classic SARC-F are being investigated [22]. However, results in validating studies are inconsistent and populations lack size [24].

2.1.2. Anthropometric measurements

Body mass index (BMI), arm and leg anthropometry, including triceps skinfold (TSF), mid-upper-arm circumference (MUAC) or calf circumference (CC) as well as different derived equations, such as mid-upper arm muscle circumference (in literature abbreviated MUAMC or MAMC) calculated with MUAC and TSF, are objective variables that are available in various clinical settings and therefore widely used [30]. For example, muscle mass might be predicted using the variables MAMC, TSF and CC [31,32]. MAMC can be calculated using the standard equation: MAMC (mm) = MUAC (mm) − [3.14 × TSF (mm)]. To evaluate the results, reference charts are used considering population, age and sex [33–35]. Data from the ilSIRENTE study indicates that low muscle mass can be classified as MAMC less than 21.1 cm in men and 19.2 cm in women [34]. For the measurement of CC, a cut-off-point of less than 31 cm was considered as low muscle mass, as it was associated with lower muscle functionality [35,36].

BMI is a well-recognized diagnostic measure for malnutrition [37], but is not suitable for predicting muscle mass as it does not differentiate between muscle and fat mass [38]. Thus, cases of malnutrition can occur in -according to the BMI- normal weight people, but are masked by an increased fat mass. As the BMI is used in some regions of the world for recognizing malnutrition, it is legitimate to be named in this context despite the described shortcomings [37].

Standard anthropometric measurements, including MUAC, MAMC or CC might involve measurement variability in practical application. Furthermore, the lack of general and international standardization and of reference values for different patients, ages or ethnic groups is a disadvantage. Nevertheless, they can be used as alternatives or complementary to apparatus-based measures like bioelectrical impedance analysis [39] or expensive techniques like MRI, as these methods are cheap, easily executed and available in most settings.

2.1.3. Muscle strength and performance: hand grip strength, chair stand test (chair rise test), gait speed, timed-up-and-go test and short physical performance battery (SPPB)

Diminished hand grip strength is associated with reduced nutritional status and considered a predictive marker of mortality and morbidity [37]. In several studies, impaired grip strength is related with prolonged length of hospital stay, postoperative complications, increased risk of readmission and poor health [37]. Therefore and due to its simple implementation, grip strength is recommended as a supportive measure in both the Global Leadership Initiative on Malnutrition (GLIM) criteria and the EWSGSOP recommendations for the diagnosis of malnutrition and as assessment of muscle mass [37]. To exclude a nutritional risk, measured hand grip should not be below 85% of the expected value, which can be calculated individually by a formula comprising age, sex and BMI (see Appendix, table 2) [40–44]. As an alternate measure the chair stand test (5-times sit-to-stand) has been suggested as a proxy for strength of leg muscles [1,2].

Gait speed is related to survival in elderly patients and seems to reflect their state of health. In addition to the musculoskeletal system, walking requires energy and various organ systems such as nervous, pulmonary, cardiac and circulatory systems. Thus, reduced gait speed can consequently be attributed to a reduced function of (one of) these systems [45]. The 4-m usual walking speed test is a common gait speed test for the assessment of physical performance [46], which is safe and highly reliable. EWGSOP2 recommends a cut-off point of $\leq$0.8 m/s as an indicator of severe sarcopenia [1,2]. Also Timed-up-and-go test or Short physical performance battery (SPPB), may be used for evaluation of physical performance [2].

2.1.4. Combined tools – screening

The Ishii screening tool is a model containing three variables: age, grip strength and calf circumference, stratified for sex. It has a relative high sensitivity when compared to the SARC-F (75.5% for women and 84.9% for men), making it more suitable as a screening tool. Its specificity (resp. 92.0% and 88.2% for women and men) is comparable to the specificity of the SARC-F (93.7%) [22]. In comparison to the SARC-F, the Ishii screening tool provides a more objective risk assessment of the probability of being sarcopenic. This tool has however not undergone external validation.

Other combined tools use the presence of two criteria to detect sarcopenia, namely decreased muscle mass and decreased muscle functionality [47]. The EWGSOP promote similar diagnostic criteria and even propose an algorithm (see Appendix, Fig. 1) [1,2]. Decreased muscle functionality is defined by low gait speed, i.e. a walking speed below 0.8 m/s in the 4-m walking test, as well as decreased handgrip strength [48]. Muscle mass is to be determined by BIA, dual x-ray absorptiometry (DXA) or anthropometric measurements including MUAC, CC and triceps skinfold thickness [1,2]. Although the algorithm was initially designed for elderly (>65 years), the algorithm can also be used for younger people at risk [1,2].

2.2. Diagnostic tools

Once screening has identified a high probability of a decreased muscle mass or function, additional tools can be used to describe muscle mass and muscle quality. These tools require a high specificity with a high internal and external validity [49]. In our opinion, in contrast with screening tools, aspects such as cost-effectiveness and availability are of secondary importance. Outcome should provide accurate and detailed information on the status of muscle mass, and preferably muscle quality, in single individuals. Inter- and intra-observer variability should be minimal [50].

2.2.1. Computed tomography (CT)

CT imaging is the current gold standard for the quantification of muscle mass in sarcopenic, cachectic and frail patients [51–56]. CT images are useful to differentiate between various tissues and evaluate body composition based on the specific attenuation of each tissue measured in Hounsfield units (HU) [51]. Despite the wide use of CT imaging for the study of sarcopenia or cachexia, a review from 2018 by Engelke et al. [53] calculating the quantitative analysis of skeletal muscle by CT imaging, found no standardized imaging protocol and the image acquisition settings varied between studies. In recent studies a series of quantitative metrics are used to describe muscle mass of patients and its relationship to healthy subjects [57,58]. The most common metrics are skeletal muscle area (SMA, cm2), skeletal muscle index (SMI, cm2/m2) and muscle radiation attenuation (MRA, HU).

All parameters are obtained based on the analysis of a single slice CT scan. SMA is the cross-sectional muscle area measured at the level of third lumbar vertebra as demonstrated in a study by Shen et al. [59]. To relate SMA to total muscle mass and obtain a relative measurement it is normalized to the square of body height, resulting in the SMI [60]. MRA, calculated as the average HU of the cross-sectional muscle area, is a measurement of muscle quality with lower values indicating higher muscle fat content [61]. Not named in the list above, but occasionally referred to is the psoas muscle index (PMI, cm2/m2) [58]. Like the SMI, the PMI is calculated by dividing the psoas muscle area observed in an L3 slice by the body height squared.

Different software is available to segment skeletal muscle in L3 scans. Most frequently used are Slice-O-Matic and ImageJ [53]. A study from van Vugt (2017) showed excellent intra-observer (Intraclass Coefficient Correlation [ICC] 0.999–1.000, $P < 0.001$) and inter-observer (ICC 0.998–0.999, $P < 0.001$) agreement for both software programs [62].

CT-scanning is the gold standard for precise measurements of skeletal muscle mass in all patients. However, fabricating and processing CT-images is a costly process as expensive hardware is used for CT-scanning. The amount of radiation patients are exposed to in CT-imaging is high compared to other techniques. Frequent scanning could pose serious threats to patient health as it increases the risk of unwanted side effects [63]. It provides however reliable data and is more prone to investigator related errors.

2.2.2. Magnetic resonance imaging

MRI is a technique that measures the magnetic properties of nuclei. These nuclei can be localized and possibly mapped as an image; they provide information about the chemical and physical environment of the nucleus. MRI can be performed using a variety of acquisition parameters which results in different types/modalities of imaging and corresponding outcome parameters [56]. The following modalities and corresponding outcome parameters are used:

MRI imaging	Outcome parameter(s)
T1	Muscle mass [64]
DIXON	Water/Fat composition of a muscle [65,66]
DTI	Structural integrity [67,68]
Proton MRS	Quantification of Muscle Fat and creatine store [69–72]
Phosphor MRS	Phosphor creatinine, Pi and pH dynamics during- and post-exercise [73–75].

MRI allows for the cross-sectional analysis of muscle quantity and quality. Depending on the modality, MRI can provide anatomical (muscle mass) plus three additional types of information: the structure of the muscle (DTI), the fat innervation of the muscle (DIXON, 1H-MRS) and fiber type composition of the muscle (31P-MRS), which gives a unique insight into the metabolic quality of the muscle.

In general, MRI/MRS is considered safe at field strengths up to and including 7T. No ionizing radiation is used in the acquisition. A study by Kiefer (2018) shows that quantification of skeletal muscle fat content and area by MRI is highly reproducible giving excellent inter-observer agreement (ICC 0.98–0.99) and intra-observer reproducibility (ICC 1.0) [39]. However, several contra-indications, such as implants, may result in exclusion of participants. Besides that, MRI is limited due to its high cost and limited availability. Its limitation also includes the long image acquisition time and operational complexity [51,52].

2.2.3. DXA (dual energy X-ray absorptiometry)

Dual-energy X-ray absorptiometry (DXA) provides precise analyses of body composition, including bone mineral density (BMD) and distribution between lean and fat masses. The principle of DXA is based on the property of X-rays to be attenuated in proportion to composition and thickness of the material the beam is passed through [32,76].

DXA images are segmented by creating body regions of interest (ROI) like arms, legs or trunk. Skeletal muscle mass is approximated by calculating lean mass. Appendicular lean mass (ALM) is the sum of lean mass of the arm and leg ROIs and is sometimes referred to as appendicular skeletal muscle mass (ASMM). Currently ASMM is the most commonly used measure to assess sarcopenia [77]. ALM index (ALMI), or ASMM index (ASMMI), are obtained by normalizing ALM, or ASMM, to the squared body height or BMI [52,78].

The International Society for Clinical Densitometry indicated that "low lean mass" could be defined using ALMI with Z-scores derived from a young adult, race, and gender matched population [79]. An ALMI value of less than 2 Z-score is the most commonly used parameter for diagnosing sarcopenia with DXA, as it is strongly associated with functional disabilities in elderly [80].

DXA may be considered as a reasonable alternative for assessing muscle mass compared to much more sophisticated, time-consuming and expensive techniques such as magnetic resonance imaging [56] and Computerized Tomography (CT) scans. A study by Moreira (2018) showed high reproducibility for body composition measurement by DXA for whole body mass (ICC 0.999) and lean mass (ICC 0.995) [81]. Furthermore, high intra-observer reproducibility for ROI measurement was observed with ICC values ranging between 0.952 and 0.999 [81]. Other studies point at the differences in materials and software, possibly influencing outcome for different systems. In contrast to CT and MRI, DXA yields two dimensional images of the whole body. Exposure to radiation associated with DXA is low (<5microSv), and highly acceptable. Nevertheless, even this low dose radiation needs to be considered as a limiting factor for routine assessment of body composition. Other limitations of this technique are high equipment costs and limited availability [82].

2.2.4. Bio-electrical impedance analysis

BIA is a non-invasive, fast and easy-to-use method for estimating body composition, with moderate acquisition and low maintenance costs, commonly used in clinical practice [82]. The BIA method is validated and useful for determining body composition at a distinct point of time, but also for the changes of body composition over a longer period of time [39]. It is applicable in various clinical settings and many devices are portable. Derived techniques based on impedance analysis have been proposed to assess muscle mass or quality, such as bioelectrical impedance vector analysis (BIVA), bioelectrical impedance spectroscopy (BIS) or electrical impedance myography (EIM). However, none of these techniques performs considerably better in clinical routine due to lack of validation, reference data, or higher methodical requirements. The basic concept is based on the different conductivities of the human body components when passing an insensible alternating current through the body. The body water is rich in electrolytes and therefore conducts the current through the body. The cells function as resistance, here called impedance (Z). Due to the structure of the body cells, the impedance comprises of two partial resistances. All impedance-derived parameters are based on these two partial resistances. Square of the body height divided by the resistance results in the total body water, which is the basis for all other BIA derived parameters [83,84]. For reliable data collection, it is important to adhere to the standardized instructions of the manufacturer (i.e. patients have to be empty-stomached, certain time interval to the last physical activity, starting measurement after a certain time of rest in a lying position) [82].

The lean body mass consist of two components, the body cell mass (BCM) including muscle mass and the extracellular mass (ECM) [85]. The ratio of ECM and BCM, the so-called ECM/BCM-index, is an early predictor of malnutrition [83]. The fat mass results from the difference between lean body mass and total body weight [83]. Apart from the ECM/BCM-index, the phase angle (PhA) is considered to be a reliable prognostic parameter for malnutrition and has been recommended as a clinical tool to monitor nutritional support [86]. A study by Jo et al. (2019) shows strong association between BIA and CT for the adjustment of skeletal muscle mass (SMM) ($p < 0.001$, correlation coefficient = 0.898 for crude SMM; $p < 0.001$, correlation coefficient = 0.858 for BMI-adjusted SMM) [87,88]. In literature different equations [1,2,83,88,89] are used for either appendicular skeletal muscle mass, whole body muscle mass, or indices mainly divided by squared body height. The EWGSOP2 consensus proposes the Sergi equation for older European populations to estimate ASMM [1,2,88].

The BIA is a non-invasive, cheap, easy and fast method to evaluate body composition without any radiation exposure [83,89]. Despite some limitations in obese and cachectic patients due to disproportion of body mass and body conductivity and a greater variety of intra- and extracellular water, BIA is validated and useful for determining the body composition at a distinct point of time as well as for monitoring the change of body composition over a longer period of time [89].

2.2.5. Ultrasound

Ultrasound can be used to analyse key parameters of skeletal muscle structure in terms of architecture (thickness, cross-sectional area, fascicle length and pennation angle) and texture [90]. Usually, the measurement is done with a high-frequency linear probe (>7 MHz). To determine the thigh muscle thickness (TMT), the measurement is made, on an axial cut, halfway between the large trochanter and the patella at the level of the thigh muscles. Besides the rectus femoris, other muscles have been used to establish the thickness such as the biceps brachii, the triceps muscles and the gastrocnemius [91,92]. A recent review on the validity of ultrasound to quantify muscles in older adults (≥60 years) reported high ICC scores ranging from 0.92 to 0.99 [93]. However only few validation studies have been published where ultrasound volumetric measurement is used without providing insight proper description of muscle quality.

Ultrasound could be a simple diagnosis method for sarcopenia, but few validation studies have been made and the heterogeneity of methodology and references limits accurate interpretation. However, ultrasound is portable, it has low costs and risk and no ionizing radiation is used [90,91].

2.2.6. Muscle biopsy

Traditionally muscle fibres are divided into three major fibre types based on the speed of shortening: type I, being slow twitch

fibres, and type IIA and IIB, respectively fast twitch oxidative and fast twitch glycolytic fibres [94]. Today there are multiple ways of classifying muscle fibres. Although known that there are more than 2 ways of classifying muscle fibres, we will maintain the type 1–2 classification in this review [95]. Type 2 fibres are crucial in reactive movements, e.g. leg movement during falling. Various studies have described the decrease of type 2 muscle fibres with aging [96,97]. Therefore a possible correlation between loss of type 2 muscle fibres and sarcopenia exists [98]. Proper investigation of muscle cells is available through muscle biopsy [99].

Not widely described as a diagnostic or screening tool for sarcopenia, muscle biopsies can provide physicians with valuable information concerning muscle quality [1,2]. Two major methods for muscle biopsy exist; open biopsy and needle biopsy. After biopsies are obtained, there are three different methods for typing muscle fibres: 'Histochemical staining for myosin ATPase', 'myosin heavy chain isoform identification', and 'biochemical identification of metabolic enzymes' [99]. With regard to identification of sarcopenic or cachectic patients, quality of muscle can be defined by the balance between different muscle types [96].

Although the evaluation of the muscle quality with muscle biopsy is excellent, the disadvantages are obvious. The invasive technique is a burden for patients and imposes risk of infection [100]. In addition, muscle biopsies require additional infrastructure and knowledge in obtaining, processing and interpretation of the data. Moreover, the evaluation only shows muscle quality, and no information on muscle function is obtained.

2.2.7. Laboratory measurements

Biochemical indices such as albumin, micronutrients, creatinine in serum and urine or creatine dilution test, amino acids, myoglobin, creatine kinase and other serological biomarkers, especially biomarker panels, are discussed in the assessment of the nutritional status and muscle mass [1,2,30,37,101,102]. To date, there are no specific recommendations, references, or cut-off values available for any specific biomarker in order to assess muscle mass or quality. Physical performance, muscle strength and muscle mass are considered the primary outcome domains [1,2].

2.3. Longitudinal monitoring

Physical exercise and nutrition intervention are effective in treatment of muscle loss [103–106]. However, the rate at which the effects take place is less well-known. An important aspect in this evaluation is the applied tools for longitudinal monitoring of treatment effects. Ideally, such a tool should be non-invasive, harmless, fast and easy, and should yield outcome parameters that are clinically relevant and are influenced by the treatment. In addition, these parameters should be highly accurate and should provide sufficient detail to detect small changes, for example in measurements that are repeated weekly or monthly [107]. Based on these criteria, the proposed tools for longitudinal monitoring are: HD-EMG monitoring, microwave imaging, functional measurements (hand grip strength and gait speed) and anthropometric measurements (MUAC, MAMC and CC).

2.3.1. High-density surface electromyographic signals (HD-EMG)

HD-EMG provide unique opportunities for non-invasively monitoring neuromuscular changes at motor unit level. HD-EMG signals are recorded from flexible and adhesive grids of electrodes placed on the skin while subjects contract their muscles at submaximal force levels [102]. EMG signals are decomposed [108] to identify and assess the activity of a large number of motor units over a wide range of torques providing direct evidence on strategies used by the central nervous system to control muscle torque [109]. The assessment of motor units action potentials (MUAP) amplitudes and MUAP conduction velocity, are actually susceptible to positive changes in the early stages of physical interventions [110,111]; individual motor units can be tracked across sessions [112] and the possibility of monitoring their properties longitudinally are well documented [113].

Hence, since Sarcopenia is associated with motor unit remodelling [114], it is reasonable to consider HD-EMG a further promising tool to noninvasively highlight the effectiveness of treatments and interventions. Therefore, HD-EMG may gather information at a level of the neuromuscular system inaccessible for other means [102,110,115]. To reach such an innovative result analysis requires sophisticated algorithms due to the complexity of the signal generated from a number of motor units and recorded from a large volume conductor [110,115,116]. This has to be considered when using this technique.

2.3.2. Microwave based quantification

Microwave sensing is a technique with promising potential for quantification of tissue properties in a variety of fields, both industrial and medical [108,109,112]. The technique uses microwave radiation to quantify tissue properties. Quantification is achieved by analysing the influence of dielectric tissue properties on the physical behaviour of the microwaves. In short, propagation, reflection and attenuation of the microwaves are all influenced by the electrical properties of the underlying tissue. Therefore, analysis of the microwave signal yields accurate information on both the quantity and the quality of tissue [16]. The contrast between bone or fat and soft tissue is visible, although the abnormalities within soft tissue is still challenging. In spite of the difficulties mentioned, it has been demonstrated that microwave based quantification is applicable for different diagnostic modalities such as breast cancer detection, diagnostics of lung cancer, brain imaging and cardiac imaging [117].

Although use of microwave sensing is emerging in medical application, current use of the technique for muscle quantification is still in the phase of validation [117–120]. Microwave sensing uses a robust technique that requires low power, has a high accuracy, is non-invasive and has excellent reproducibility. Besides that, the nature of the radiation is non-ionizing making it possible to repeatedly measure tissue properties without the risk of negative effects. This is an important advantage over golden standards such as CT-scanning and X-ray imaging [113], making it suitable for monitoring of treatment effects. Although validation for the detection of sarcopenia is still ongoing, early clinical data are promising [113]. Due to the reproducibility, the ease of use and harmless methodology it appears to be a suitable tool for monitoring.

2.3.3. Functional measurements and anthropometric measurements

Functional measurements (hand grip strength and gait speed) and anthropometric and laboratory measurements (MAMC, CC and biochemical indices) are already been described extensively under screening tools. These tools are quick and safe, making them suitable for regular measurements. Outcome parameters show overtime clinical progress influenced by treatment. However, to our knowledge no studies have been performed to investigate the sensitivity of longitudinal monitoring of muscle mass using functional and anthropometric measurements.

3. Discussion

Sarcopenia is associated with significant health risks and therefore early identification and adequate diagnosis is recommended.

Several groups have defined criteria for sarcopenia, including the recently revised criteria from the European Working Groups on Sarcopenia in Older People (EWGSOP2). Unfortunately, agreement between definitions is poor, and although a wide variety of tools for muscle mass estimation is currently available, the translation to clinical decision-making is not always straightforward. The proper use of tools depends on their specific technical requirements, but also on the clinical scenario in which they are applied. A structured approach to decide what tool to use in which scenario is currently lacking. In this review we therefore summarize the commonly used tools for quantification of muscle mass or quality in three different clinical scenarios: screening, diagnosis and longitudinal monitoring. In addition, we present new promising techniques for muscle mass quantification. An overview of described diagnostic tools and their strengths and drawbacks is presented in Appendix table 3.

3.1. Screening

Tools used for screening require high sensitivity and should be widely available, user-friendly, efficient, non-invasive and cheap. Several tools meet these requirements, specifically the SARC-F questionnaire, mid-arm muscle circumference (MAMC), calf circumference (CC), hand grip strength and gait speed. However, the combination of different tools to identify low muscle mass increases sensitivity even further. In our view such a combination should include a questionnaire and a tool for both muscle mass and muscle functionality. We therefore recommend the use of the SARC-F in combination with CC or MAMC and in combination with hand-grip strength or gait speed. This recommendation in accordance with the proposals made by the Ishii group [22] and the EWGSOP group [1,2].

3.2. Diagnosis

Tools used for diagnosis of decline in muscle mass and sarcopenia require a high specificity with a high internal and external validity. CT scanning is still considered the gold standard for diagnosing sarcopenia [1,2,51–56]. Inconsistent use of cut-off points in different studies, high medical costs, and the radiation burden are important drawbacks. MRI is considered a safe alternative as it does not use ionizing radiation and it provides additional information on muscle quality. However, the complexity, costs, and contra-indications for MRI render it less suitable for the assessment of muscle mass in clinical practice [51].

DXA might be a reasonable alternative for assessing muscle mass, since radiation exposure is low. Limitations for DXA are high equipment costs, lack of portability and limited availability.

BIA is regarded by many as a helpful diagnostic modality for muscle mass quantification. It is relatively cheap, harmless and commercial clinical devices are already easily accessible. Caution should be taken in interpretation of data, since results are influenced by multiple external factors. In addition, the outcome of BIA is unreliable in the extremes of nutritional status.

In summary, for diagnosis of sarcopenia CT scanning is still the gold standard. Especially in patients undergoing a CT scan for other purposes, data for quantification of muscle mass can be easily extracted. However, depending on local availability and expertise, MRI, DXA, and BIA can be cautiously used as alternatives.

3.3. Monitoring

Tools for longitudinal monitoring should be non-invasive, fast and easy, should give clinically relevant parameters and should detect small changes in order to evaluate treatment effects over time. Functional measurements (hand grip strength and gait speed) combined with anthropometric measurements (MAMC and CC) meet these criteria and are therefore widely recommended but are not appropriate to assess muscle mass [33–35]. Moreover, it is important to realize that these are quantitative and functional tools without specification of changes in muscle quality. Furthermore, it remains to be seen whether these tests are sensitive enough to discriminate small changes over short time periods. HD-EMG- and microwave imaging are relatively new but promising tools for the monitoring of muscle mass as well as muscle quality. Both tools are non-invasive and give reliable information about the characteristics of the muscle. However, clinical studies for (repetitive) measurements of muscle mass are scarce and additional clinical validation is needed.

4. Conclusion/implications for practice

With the current knowledge we recommend the combination of at least one anthropometric and one functional measurement for longitudinal monitoring of muscle mass. The introduction of new accurate techniques, specifically microwave-based imaging, would greatly facilitate longitudinal monitoring.

In conclusion, this narrative review proposes different modalities for muscle mass quantification in different clinical scenarios. It supports clinical decision-making in choosing the right tools for muscle mass quantification depending on the need within a given clinical scenario as well as the local availability and expertise.

Ethical guidelines

All the principles of ethical authorship and publishing in the Clinical Nutrition ESPEN are certified.

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Author contributions

Conceptualization LLGCA, SCB, OC, RJR, EG, AB, TJB; Funding acquisition SCB, OC, RJR, EG, AB, TJB; Investigation & Methodology LLGCA, JR, MB, AS, SCB, OC, GCT, RJR, EG, PSG, AR, GB, KWR, JATB; Project administration LLGCA, JR, KWR, JATB, TJB; Supervision SCB, OC, RJR, EG, AB, TJB; Visualization LLGCA, JR, MB, AS, SCB, OC, GCT, RJR, EG, PSG, AR, GB, KWR, JATB, TJB; Roles/Writing - original draft; LLGCA, JR, MB, AS, SCB, OC, GCT, RJR, EG, PSG, AR, GB, KWR, JATB, TJB; Writing - review & editing LLGCA, MB, AS, SCB, OC, GCT, EG, PSG, AR, GB, JATB, TJB.

Declaration of competing interest

There is no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnesp.2022.01.027.

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